

PTO 10-1038

WO
20001214
A1
0074755

DEVICE FOR TREATING SLEEP-RELATED RESPIRATORY DISORDERS AND METHODS
FOR THE CONTROL THEREOF
[Appareil de Traitement des Troubles Respiratoires du Sommeil et son Procédé de Commande]

Enrique Vega et al.

UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. DECEMBER 2009
TRANSLATED BY: MCELROY TRANSLATION COMPANY

PUBLICATION COUNTRY (19): WO
DOCUMENT NUMBER (10): 0074755
DOCUMENT KIND (12): A1
PUBLICATION DATE (43): 20001214
APPLICATION NUMBER (21): PCT/FR00/01505
APPLICATION DATE (22): 20000531
INTERNATIONAL CLASSIFICATION⁷ (51): A 61 M 16/00
PRIORITY COUNTRY (30): FR
PRIORITY NUMBER (30): 99/07189
PRIORITY DATE (30): 19990608
LANGUAGE OF SUBMISSION (25): French
LANGUAGE OF PUBLICATION (26): French
INVENTORS (72) (75): Enrique Vega et al.
APPLICANT (71): TAEMA

DESIGNATED CONTRACTING STATES

(national): (81): AE, AL, AU, BA, BB, BG, BR, CA, CN, CU,
CZ, EE, GD, HR, HU, ID, IL, IN, IS, JP, KP,
KR, LC, LK, LR, LT, LV, MG, MK, MN, MX,
NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, US,
VN, YU, ZA.

DESIGNATED CONTRACTING STATES

(regional): (84) European Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

TITLE (54): DEVICE FOR TREATING SLEEP-RELATED RESPIRATORY DISORDERS AND METHODS FOR THE CONTROL THEREOF

FOREIGN TITLE [54A]: Appareil de Traitement des Troubles Respiratoires du Sommeil et son Procédé de Commande

The invention relates to an artificial ventilation apparatus intended for the treatment of sleep-related sleep respiratory disorders, especially sleep apnea, and to a method for the control of such an apparatus.

When it is necessary to determine the operating parameters of an artificial ventilation apparatus that are the most appropriate for a patient suffering from sleep-related respiratory disorders, especially sleep apnea or hypopnea, it is usually necessary for this patient to spend several nights in a sleep laboratory during which he is continuously monitored and studied.

More precisely, the patient who suffers from a sleep-related disorder must spend a first night in the sleep laboratory, during which the existence of any sleep-related disorders is diagnosed by means of a polysomnograph, and the number of respiratory events or sleep-related disorders occurring during sleep is determined.

Finally, after this first night of diagnostics, the patient must spend a second night in the sleep laboratory, during which a technician is in charge of determining the appropriate effective pressure for the treatment of the patient.

For this purpose, the technician in charge of finding this effective pressure monitors the patient constantly throughout the entire night, gradually changing the pressure of the gas sent to the patient during his/her sleep until a pressure level is reached at which the respiratory events, i.e., the sleep disorders, start to disappear.

This pressure level corresponds to the effective treatment pressure, which is generally approximately 4-18 mbar.

Now, it immediately clear that this method is not practical, for the patient who has to spend several nights away from home, or for the technician in charge of monitoring the sleeping patient and thus required to stay awake throughout the entire night. /2*

The purpose of the present invention is then to attempt to overcome the above problems and disadvantages by proposing an artificial ventilation apparatus intended for the treatment of sleep-related respiratory disorders, particularly sleep apnea, that is self-adapting, and a method for controlling such an apparatus.

In other words, the purpose of the invention is to propose a method for the automatic control of the variations of the pressure of the gas sent to the user while he/she is sleeping, i.e., a method for the control of the respiratory assistance apparatus that does not require the intervention of a technician, a physician or other similar person, and that is able to adapt to the respiratory events of the user and/or take into account the duration of the different sleep periods.

The invention thus concerns a respiratory assistance apparatus, preferably of the Continuous Positive Pressure type, comprising:

- at least one gas duct that can be connected to the upper airways of a user in the sleep phase,
- at least one turbine to supply said gas duct with a respiratory gas at substantially constant pressure,
- means for the fixation and/or memorization of the desired duration (t),
- means for the fixation and/or memorization of the desired pressure,
- means for the fixation and/or memorization of a desired threshold number (ns) of respiratory events,
- means for the determination of respiratory events to determine the total number (n) of respiratory events that occur in the user during the preestablished duration (t),

* [Numbers in right margin indicate pagination of the original text.]

- calculation means to compare the total number (n) of respiratory events, which is determined by said means for determining respiratory events, with the prefixed threshold number (ns) of respiratory events, and

- control means allowing the control of the turbine to deliver, for the prefixed duration (t), /3
gas at the desired pressure, and to maintain or modify said pressure of the gas delivered by said turbine by acting on said turbine in response to the calculation means.

It is preferred for said apparatus to comprise, in addition, means for the fixation and/or memorization of a pressure variation value (ΔP) of 0-50 mbar, preferably 0-30 mbar, and/or means for the fixation and/or memorization of at least one type of respiratory event.

Moreover, the invention also relates to a method for the control of a respiratory assistance apparatus according to the invention, which comprises at least one turbine to supply at least one gas duct with a respiratory gas at substantially constant pressure, where said gas duct can be connected, in addition, to the upper airways of a user in the sleep phase, in which one proceeds according to the following steps of:

- (a) control of the turbine to deliver, for a prefixed duration (t), gas at a desired pressure,
- (b) determination of the total number (n) of respiratory events that occur in the user for the prefixed duration (t),
- (c) comparison of the total number (n) of respiratory events, which is determined in step (b), with a prefixed threshold number (ns) of respiratory events, and
- (d) maintenance or modification of the pressure of the gas delivered by said turbine by acting on said turbine as a function of the comparison of step (c).

Depending on the case, the method according to the invention can comprise one or more of the following claims:

- in step (d), one controls the turbine to increase the pressure of the gas delivered by said turbine, if in step (c) it is determined that $n > ns$.

- in step (d), one controls the turbine to maintain substantially constant the pressure of the gas delivered by said turbine, if in step (c) it is determined that $n \leq ns$.

- in step (d), one controls the turbine to increase the pressure of the gas delivered by a pressure variation value (ΔP) such that $0 < \Delta P \leq 50$ mbar, preferably $0 < \Delta P \leq 30$ mbar.

- after an increase in the pressure of the gas according to step (d), one repeats the steps (a)-(d) as many times as necessary until the total number (n) of respiratory events determined in step (b) is less than the prefixed threshold number (ns) of respiratory events. /4

- it comprises, in addition, at least one step of memorization of at least one parameter chosen from the group consisting of the duration (t), the total number (n) of respiratory events, the threshold number (ns) of respiratory events, and the pressure variation value (ΔP).

- it comprises, in addition, at least one step of fixation of at least one type of respiratory events to be determined in step (b).

- at least one type of respiratory events is chosen from the group comprised of apnea (AP), hypopnea (HP), periods and/or times of snoring (SR), and other respiratory events (ORE).

- the total number (n) of respiratory events is equal to the sum of the number of respiratory events of one type or another that occur during the duration (t).

- the prefixed duration (t) is between 10 sec and 1 h, preferably 1 min and 30 min, preferably between 3 and 10 min, and more preferably on the order of 6 min.

- in step (a), the pressure is 2-20 mbar, preferably 2-12 mbar, preferably 3-8 mbar.

The invention is described below in further detail in reference to the figures in the appendix, which are given as illustrations but not limiting.

In Figure 1, an algorithm is diagrammed that represents the procedure of operation of the ventilator according to the invention.

The control method according to the invention is carried out, as shown in Figure 1, and explained below.

During a first phase (1, 2), one controls the turbine of the respiratory assistance apparatus so that it delivers respiratory gas, such as air or oxygen-enriched air, at a substantially constant pressure (at 1), for a prefixed duration t , for example, a duration of up to 120 min, during which one measures or determines (at 2) the total number n of respiratory events that occur in the user over the prefixed duration t . /5

It is preferred for the pressure to be fixed at a low pressure value, for example, 4 mbar, which allows the patient to fall asleep without being in discomfort due to an excessively high gas pressure.

The respiratory events that are determined are apnea, hypopnea, snoring periods, and other respiratory events entailing a decrease in respiratory flow.

The total number n of respiratory events that occur during the period t is memorized by the machine and compared (at 2) with a prefixed threshold number ns of respiratory events, and the result of this comparison is used to maintain or, conversely, modify the pressure of the gas delivered by the turbine.

Thus, if the number n is less than the threshold number ns , then the pressure level is maintained at its initial value, for example, 4 mbar (loop B1 in Figure 1), because, in this case, either the fixed pressure level is sufficient to be effective from the therapeutic point of view, or the subject is not or only slightly subject to respiratory disorders requiring a more powerful treatment.

In contrast, if the number n is greater than or equal to the threshold number ns , then the pressure level is increased by a pressure variation value ΔP such that $0 < \Delta P \leq 50$ mbar, preferably $0 < \Delta P \leq 30$ mbar,

for example, 4 mbar, until a pressure level is reached (at 3) that is greater than the previous level, for example, a pressure level that is greater by 8 mab [sic; mbar] in this example.

Indeed, in this case, the fact that n is greater than or equal to the threshold number ns signifies that the pressure delivered by the turbine is not sufficiently high for an effective action against the sleep disorders; the pressure therefore must be increased.

The increase in the pressure of the gas delivered by said turbine is achieved by controlling the voltage of the current that supplies the turbine, by means of the control means, and by measuring the pressure, preferably close to the mouth of the user, and comparing it with the nominal pressure.

When this higher pressure level (8 mbar) is reached, the second phase begins, during which /6 one proceeds by repeating the previous step (of the first phase), i.e., one maintains (at 3), for a duration t' equal to or not equal to t , for example, 6 min (at 4), the pressure level at 8 mbar, and one counts, during this duration t' , the total number n' of respiratory events that occurred during the duration t' .

This total number is memorized at 10 (loop B2), and compared (at 5) with the prefixed threshold number ns of respiratory events, and the result of this comparison is used, as above, to maintain (loop B3), or, conversely, to modify the pressure of the gas delivered by the turbine.

Indeed, this 6-min period is a short phase of testing the effectiveness of the pressure that has been reached (8 mbar).

After the 6 min, if the number n' is greater than the threshold number ns , then the pressure is increased (at 11) very slightly, for example, by 1 mbar (loop B3), and then the steps 3, 4 and 5 are repeated until the number n' of respiratory events becomes less than or equal to the threshold number ns . For example, one can repeat the loop B3 3 times before reaching $n' \leq ns$; in this case, the pressure has increased by 1 mbar at each repetition of the loop B3, and the effective pressure obtained is thus 11 mbar (8 mbar + 3 x 1 mbar).

Once the second test phase is completed, i.e., when the pressure of the gas has reached its effective value, for example, 11 mbar, the third phase begins, which is a phase of greater duration than the previous phase, for example, 36 min, during which one maintains the pressure at its effective value (at 6), and one detects and memorizes any respiratory events.

Such a duration makes it possible to monitor a large proportion of the current sleep stage with a pressure level (at 7) that is maintained substantially constant, in such a way as to be able to verify and/or validate that the pressure obtained (11 mbar, for example) is indeed the effective treatment pressure for the patient.

Again, one compares (at 8) the number n'' of respiratory events detected during these 36 min with a prefixed threshold number ns'' (ns'' , ns' and ns may be equal or different).

If the number n'' is greater than the threshold number ns'' , then one proceeds according to loop B5, which returns to the previous loop B3 to repeat the above procedures (second phase and third phase). /7

On the other hand, if the number n'' is less than or equal to the threshold number ns'' , then one proceeds along the loop B6, i.e., one decreases the pressure by a low value, for example, 1 mbar (at 12), and then one repeats the procedures of the second phase and the third phase.

This makes it possible to correctly adjust the pressure level, and thus to verify that the pressure level has not been increased excessively during the previous second phase.

The preceding phases are repeated as many times as necessary.

It can be understood immediately that such a method is particularly advantageous because it is self-adapting, i.e., because the effective pressure level is chosen automatically by the ventilation machine and consequently no longer requires any intervention by a technician at nighttime, and it can be used at home by the patient himself or herself.

In other words, the machine adapts itself to any variation in the pressure level that is required by the patient, taking into account the time spent at a given pressure, the number of respiratory events that occurred at this given pressure level, the given pressure level itself, as well as any accidental leaks of the mask and/or unintentional disconnection of the mask.

From there, by analyzing the number of respiratory events at each pressure, an effective pressure level can be and is determined for the entire night, and this for each one of the respiratory events taken separately, or, conversely, in groups, i.e., an effective pressure level that allows the obtention of the — preferably complete — disappearance of apnea (AP) and/or hypopnea (HP) and/or ORE and/or of the snoring....

All of this is carried out on an a priori basis, as a function of the detection strategy chosen before the start of the titration session.

In Figure 2, a diagram is shown of the respiratory flow rate curve of a person who suffers from sleep-related respiratory disorders with periods of hypopnea (HP), where hypopnea is characterized by a 50% decrease in the amplitude of the respiratory flow rate of this person for a variable time period during his/her sleep. As one can see in Figure 2, during the hypopnea period (HP), the amplitude of the respiratory flow rate is only 30-40% of the normal respiratory flow rate ('NORMAL'). It should be emphasized that, when the reduction of the amplitude of the respiratory flow rate of the person reaches 90% or more, one speaks of sleep apnea (AP).

Moreover, Figure 3, as far as it is concerned, illustrates the respiratory flow rate curve of a person suffering from a third type of respiratory events that generate sleep-related respiratory disorders, namely respiratory events that do not involve a 50% to nearly 100% reduction of the respiratory flow rate, as in the case of hypopnea and apnea, respectively, but that generate a reduction in the respiratory volume by only approximately 15-50%, throughout the duration of the event, followed by resumption of respiration

and a micro-awakening of the person at the end of the event. During the resumption of breathing and the micro-awakening, one observes a large increase in the volume of the respiratory gas inspired by the person. Such respiratory events correspond to periods of flow limitation and they are referred to as ORE type events, which stands for Other Respiratory Events, which makes it possible to distinguish them from apnea (AP) and hypopnea (HP).

Figure 4, as far as it is concerned, represents the pressure variations of the gas delivered by the ventilation apparatus as a function of time, when one controls said apparatus using a control and regulation method according to the present invention.

More precisely, the automatic definition of the effective pressure level can be carried out according to the following phases.

Phase 1:

First, one inhibits any detection of respiratory events for a prefixed duration, for example, 20 min, and this by maintaining or adjusting the pressure of the gas at a low pressure value P1, for example, 4 hPa by default.

At the end of this period of inhibition, one starts a detection of the number n of respiratory events (AP, HP or ORE) for a prefixed and/or settable duration T1, for example, 120 min, and one compares the total number n of respiratory events determined in this way with a prefixed threshold number ns of respiratory events, for example, ns = 4.

/9

If $n \leq ns$, then one resets the event counter to 0, and one starts the operation again while maintaining the pressure P1.

Conversely, if $n > ns$, then one modifies the pressure of the gas delivered by said turbine by acting on said turbine to increase ($\Delta P1$) the pressure of the gas to a higher pressure value $P2$, for example, 6 hPa by default, but, preferably, this pressure value $P2$ is settable or adjustable.

The slope of the rise in the pressure ($\Delta P1$) corresponds to approximately 1 hPa per 3 respiratory cycles (duration of the inspiration + duration of the expiration).

Phase 2:

The pressure of the gas is stabilized at the value $P2$ for a prefixed duration $T2$, for example, 6 min by default, during which one detects a total number n of respiratory events for this pressure $P2$.

At the end of this period $T2$, one compares, as above, the total number n' of respiratory events so determined with a prefixed threshold number ns' of respiratory events, for example, $ns' = 2$.

If $n' \leq ns'$, then one repeats the operation while maintaining the pressure $P2$ as long as the total number n' of respiratory events is not greater than ns' .

On the other hand, if one determines that $n' > ns'$, then one modifies the pressure of the gas delivered by said turbine by acting on said turbine to increase the gas pressure as many times as necessary ($\Delta P2$ or $\Delta P3$), until a pressure value $P3$ or $P4$, for example, 8 hPa, is reached, at which the total number n'' of respiratory events for this pressure $P3$ or $P4$ remains less than ns' for a duration $T3$, preferably $T2 = T3$.

Phase 3:

The pressure of the gas is maintained at the value $P4$ for a duration $T4$ that is longer than $T2$ or $T3$, for example, for 26 min by default. It is preferred for the duration $T4$ to be settable. /10

After this duration $T4$, one compares, as above, the total number n''' of respiratory events that occurred during $T4$ with a prefixed threshold number ns''' of respiratory events, for example, $ns''' = 5$.

If $n'' \geq ns''$, then one increases the pressure of the gas slightly, for example, by 1 hPa.

However, in most cases $n'' \leq ns''$, and in that case one should decrease the pressure ($\Delta P4$) to a predetermined, preferably settable, quantity, for example, 1 hPa, to then increase the pressure to a pressure value that is slightly less than P5.

Then, one repeats the test process at this pressure value P5, by increasing ($\Delta P5$) the pressure again, if necessary, to a pressure value P6 that is greater than P5, preferably to the value P4, or, depending on the case, by validating the pressure level P5.

In other words, one determines, during each subsequent time period T5, T6..., the number of respiratory events that occur at the pressure level considered, P5, P6..., and one modifies the pressure level of the gas delivered by the turbine accordingly.

However, it should be noted that if one determines, during a time period, that the number of respiratory events occurring at the pressure level considered is greater than the fixed threshold number (for example, 5 events), it is not necessary to wait for the end of the time period considered to increase the pressure of the gas.

Indeed, for the purpose of safety and effectiveness, it is preferred to proceed to an increase in pressure (increment of 1 hPa, for example) as soon as the counter detects that the number of respiratory events that occurred is greater than the fixed threshold number, and this without waiting for the end of the time duration under consideration.

Claims

/11

1. Respiratory assistance apparatus comprising:

- at least one gas duct that can be connected to the upper airways of a user in the sleep phase,
- at least one turbine to supply said gas duct with a respiratory gas at substantially constant pressure,

- means for the fixation and/or memorization of the desired duration (t),
- means for the fixation and/or memorization of the desired pressure,
- means for the fixation and/or memorization of a desired threshold number (ns) of respiratory events,
- means for the determination of respiratory events to determine the total number (n) of respiratory events that occur in the user during the preestablished duration (t),
- calculation means to compare the total number (n) of respiratory events, which is determined by said means for determining respiratory events, with the prefixed threshold number (ns) of respiratory events, and

- control means allowing the control of the turbine to deliver, over the prefixed duration (t),
gas at the desired pressure, and to maintain or modify said pressure of the gas delivered by said turbine by acting on said turbine in response to the calculation means,
characterized in that the control means control the turbine in such a way as to increase the pressure of the gas delivered by said turbine, without waiting for the end of said duration (t) under consideration, if the comparison performed by the calculation means determines that the number of events that occurred during a part of said prefixed duration (t), at the pressure level considered, is greater than said prefixed threshold number (ns).

2. Apparatus according to Claim 1, characterized in that it comprises, in addition, means for the fixation and/or memorization of a pressure variation value (ΔP) of 0-50 mbar.

3. Apparatus according to one of Claims 1 or 2, characterized in that it comprises, in addition, means for the fixation and/or memorization of a pressure variation value (ΔP) of 0-30 mbar.

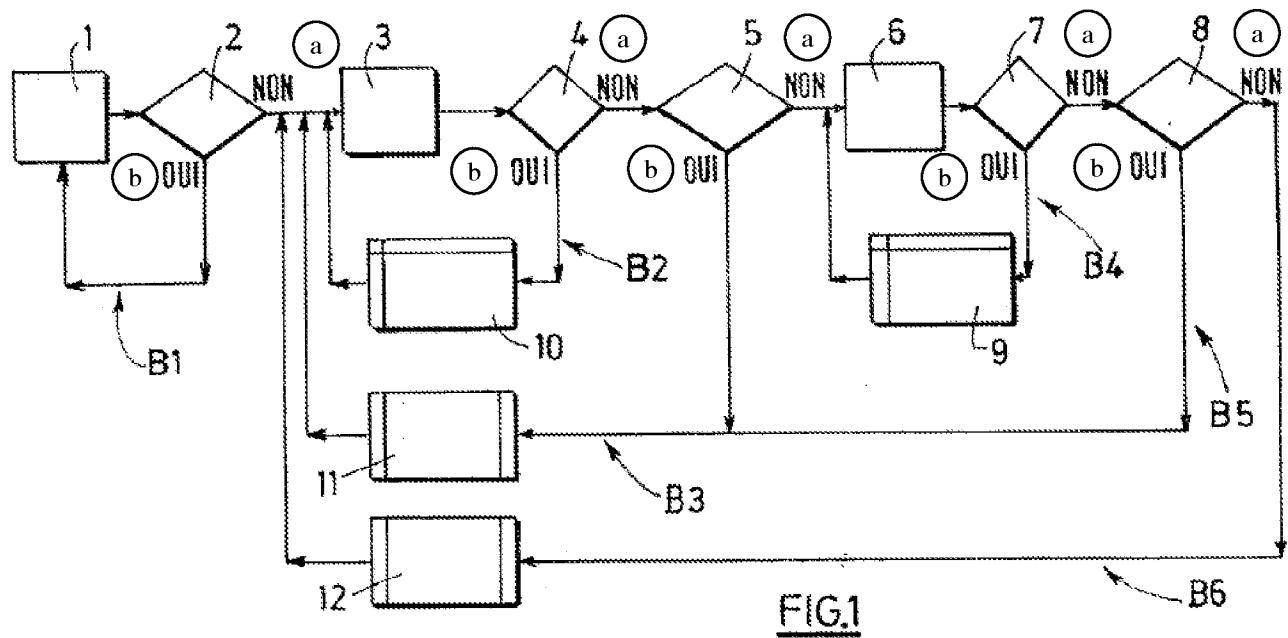
4. Apparatus according to one of Claims 1-3, characterized in that it comprises, in addition, means for the fixation and/or memorization of at least one type of respiratory events.

5. Apparatus according to Claim 1, characterized in that the control means control the turbine to increase the pressure of the gas delivered by said turbine when it is determined that $n > n_s$.

6. Apparatus according to Claim 1, characterized in that the control means control the turbine to maintain a substantially constant pressure of the gas delivered by the turbine, when it is determined that $n \leq n_s$.

7. Apparatus according to Claim 1, characterized in that the control means control the turbine to increase the pressure of the gas delivered by a pressure variation value (ΔP) such that $0 < \Delta P \leq 50$ mbar, preferably $0 < \Delta P \leq 30$ mbar.

8. Apparatus according to one of Claims 1 or 5, characterized in that the control means control the turbine by controlling the voltage of the current supplying the turbine, and by measuring the pressure, preferably close to the mouth of the user, and comparing it with the nominal pressure.



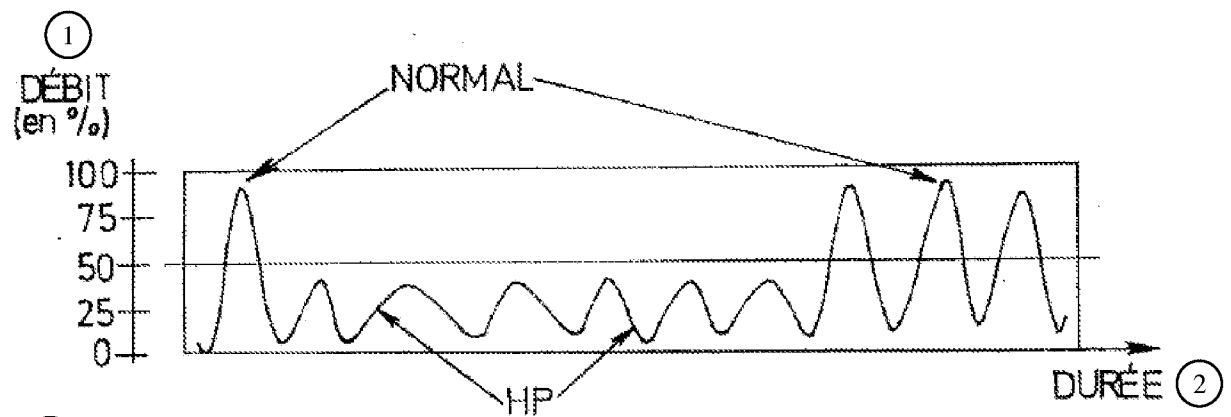


FIG.2

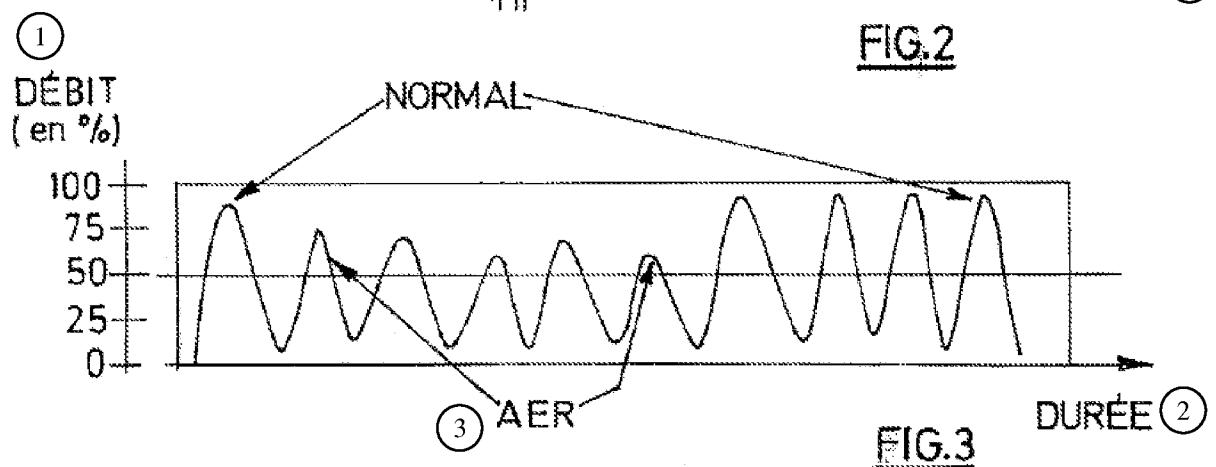


FIG.3

Key: 1 Flow rate (in %)

2 Duration

3 ORE

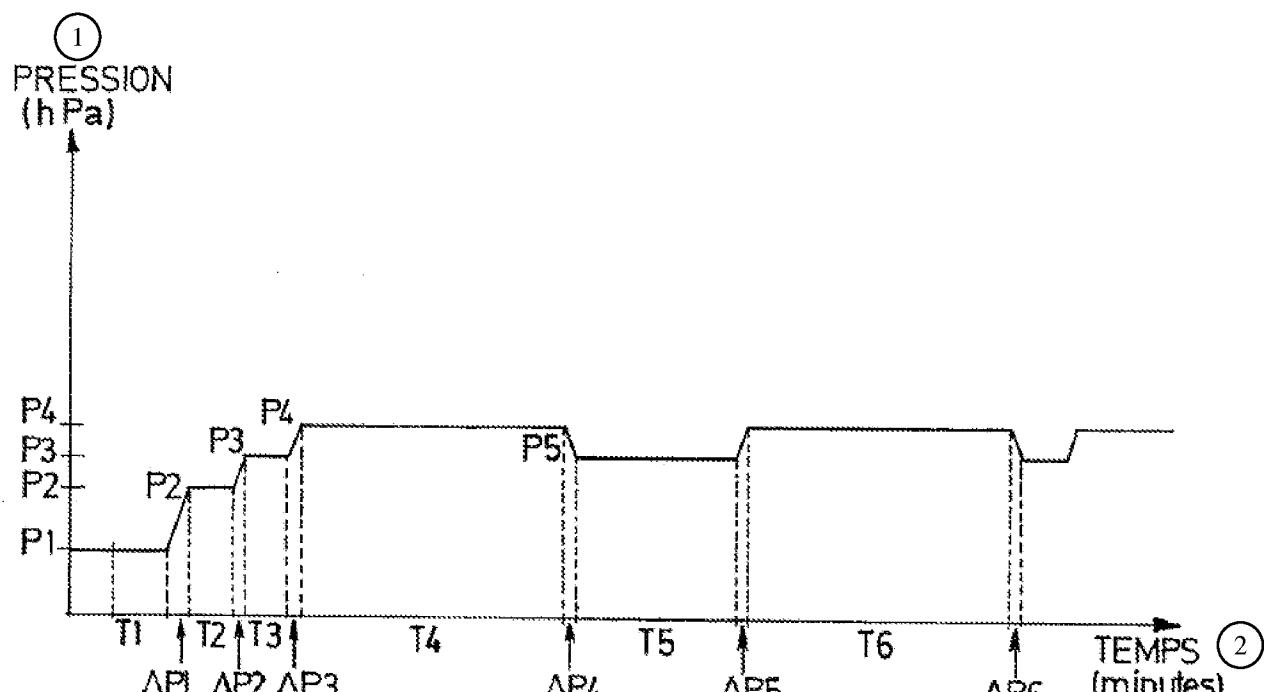


FIG.4

Key: 1 Pressure (hPa)

2 Time (min)

INTERNATIONAL SEARCH REPORT

In International Application No
PCT/FR 00/01505

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched: classification system, followed by classification symbols:
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search: name of data base and, where practical, search terms used

EPD-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 23780 A (RESPIRONICS INC) 27 October 1994 (1994-10-27) page 5, line 33 -page 7, line 4; figure 1 page 8, line 6 -page 9, line 4	1-8
X	WO 92 22244 A (AXE JOHN R ;BEHBEHANI KHROSROW (US); BURK JOHN R (US); LUCAS EDGAR) 23 December 1992 (1992-12-23) page 4, line 18 - line 26; figures page 8, line 13 -page 9, line 19	1-8
X	WO 97 26838 A (UNIV NEW YORK) 14 August 1997 (1997-08-14) page 4, line 13 -page 7, line 2; claims 18,22,29,37; figures page 12, line 15 -page 13, line 26 page 14, line 16 -page 28, line 17 ----- -----	1-8

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *B* earlier documents but published on or after the international filing date
- *C* document which may throw doubt on priority (claimed) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *D* document referring to an oral disclosure, use, exhibition or other means
- *E* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

K document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

M document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

S document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

5 September 2000

13/09/2000

Name and mailing address of the ISA

European Patent Office, P.O. Box 8000
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2340, Fax. 31 851 890 61
Fax. (+31-70) 340-2346

Authorized officer

Zeinstra, H

Form PCT/ISA/210 (second sheet) (July 1992)

page 1 of 2

12/1/2009, EAST Version: 2.4.1.1

INTERNATIONAL SEARCH REPORT

In International Application No
PCT/FR 00/01506

C) (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 722 747 A (DEVILBISS HEALTH CARE INC) 24 July 1996 (1996-07-24) column 6, line 11 - line 56; figures 1,8 column 18, line 19 -column 20, line 32 ----- WO 92 11054 A (PURITAN BENNETT CORP) 9 July 1992 (1992-07-09) page 22, line 15 -page 25, line 11; figures 16,17 -----	1
A		1

Form PCT/ISA2000 (continuation of second sheet (July 1998))

page 2 of 2

12/1/2009, EAST Version: 2.4.1.1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.
PCT/FR 00/01505

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9423780 A	27-10-1994	US 5458137 A AU 686157 B AU 6629694 A CA 2159336 A EP 9699085 A JP 8512218 T US 6085747 A	17-10-1995 09-02-1998 08-11-1994 27-10-1994 06-03-1996 24-12-1996 11-07-2000
WO 9222244 A	23-12-1992	US 5203343 A AT 163845 T AU 656292 B AU 2189292 A CA 2111324 A DE 69224745 D DE 69224745 T EP 9592492 A ES 2116338 T JP 6509487 T US 5458137 A US 6085747 A	20-04-1993 15-03-1998 27-01-1995 12-01-1993 23-12-1992 16-04-1998 06-08-1998 20-04-1994 16-07-1998 27-10-1994 17-10-1995 11-07-2000
WO 9728838 A	14-08-1997	US 5803066 A AU 1953597 A CA 2245869 A EP 9956666 A JP 20000504602 T	08-09-1998 28-08-1997 14-08-1997 17-11-1999 18-04-2000
EP 0722747 A	24-07-1996	US 5551419 A AU 712628 B AU 1318199 A AU 703829 B AU 4846395 A AU 709870 B AU 9323898 A BR 9505908 A CA 2163855 A	03-09-1996 11-11-1999 22-04-1999 01-04-1999 20-06-1996 09-09-1999 21-01-1999 23-12-1997 16-06-1996
WO 9211054 A	09-07-1992	US 5134995 A AT 190230 T AU 686034 B AU 4071195 A AU 6371798 A AU 663054 B AU 8215491 A CA 2097502 A,C CA 2206784 A DE 69132630 D EP 0563044 A EP 0968734 A ES 2145739 T JP 2927958 B JP 6503484 T US 5549106 A US 5794614 A US 5845636 A US 5259373 A	04-08-1992 15-03-2000 29-01-1998 18-04-1996 30-07-1998 28-09-1995 22-07-1992 22-06-1992 22-06-1992 13-04-2000 06-10-1993 05-01-2000 16-07-2000 28-07-1999 21-04-1994 27-08-1996 18-08-1998 08-12-1998 09-11-1993

Form PCT/ISA/10 (Intel. family search) (July 1992)